REMARKS

In view of the amendments and remarks that follow, Applicants respectfully submit that the application is in condition for allowance. Accordingly, applicants request reconsideration of the application, withdrawal of the objections and rejections of record and issuance of a Notice of Allowance.

Applicants again would like to thank Examiner Russel for his time and courtesy during the personal interview on July 1, 2003. A Communication summarizing the interview was previously submitted.

Claims 1-32 and 35-39 are pending in the application. Claims 1-14, 30 and 35-39 are rejected and Claims 15-29, 31 and 32 are objected to for the reasons of record. Claims 30-32 have been cancelled and new claims 40-42 have been added to limit cancelled claims 30-32 based on the restriction requirement. Claims 1, 4, 5 and 15 have been amended in response to the various objections noted in Paper No. 14. The amendments and new claims are not considered to involve the addition of new matter and entry of the amended claims is respectfully requested.

A new substitute specification is being submitted herewith in order to correct the SEQ ID NOS to comply with the sequence rules. No new matter is contained within the substitute specification or sequence listing submitted with this response.

The examiner has noted that the Sequence Listing filed August 15, 2003 is not approved because "[n]umerous amino acid sequences recited in the specification and claims subject to he sequence disclosure rules are not found in the proposed new sequence listing". The examiner points to the elected sequence saying that the elected sequence comprises 7 amino acids and SEQ ID NO 52 of the proposed new sequence has only 4 amino acid residues.

Applicants respectfully disagree that amino acid sequences subject to the disclosure rules are not found. For example, the elected sequence includes O-benzyl which is not an amino acid subject to the disclosure rules. Therefore, the only searchable sequence is the 4 amino acids E-P-L-G as noted in SEQ ID NO 52. The O-benzyl portion is not included in the amino acids list or in the list of modified and unusual amino acids that are subject to the disclosure rules. Therefore, the portion of the elected sequence that

needs to be included is the 4 amino acids as noted. Applicants submit that the listing filed August 15, 2003 with the proper statement of new matter is correct and should be approved.

The subject specification filed August 15, 2003 was not entered because a clean copy as required by 37 CFR 1.125 was not submitted. Additionally, the office action notes that the substitute specification as proposed would result in the presence of numerous amino acid sequences which are subject to the disclosure rules but are not recited in the proposed new sequence listing or identified by SEQ ID NOS as required. Finally, the office action notes that the substitute specification uses the language "provided as SEQ ID NO:" rather than the standard sequence identification language.

Applicants respectfully submit that the subject specification being submitted with this Request for Continued Examination is proper. A clean copy is being submitted with the required marked-up copy. Additionally, as noted above, Applicants submit that all amino acid sequences subject to the disclosure rules are properly identified in the substitute specification. In response to the question regarding the terminology used, this terminology is being used to indicate that the particular sequence is located within a sequence that may not be subject to the disclosure rules. This language was suggested by personnel at the PTO to indicate that a portion of the sequence was subject to the disclosure rules even if the entire sequence is not.

Applicants submit that the substitute specification is proper, contains no new matter and should be approved.

The office action notes that the proposed amendment filed August 15, 2003 incorrectly lists the status of claims 33 and 34. Amendment to the listing of claims in this response has been made to correct the status of these claims.

The office action notes that the proposed amendments to the claims are in improper format. All of the noted informalities have been corrected in the listing of claims which is part of this response.

The office action notes that proposed new claims 40-42 raise new issues under 35 USC 112, second paragraph. In particular, the language is considered unclear.

Applicants have amended new claims 40-42 to clarify that E^{cp} is R-γ-E-P-L-G-(O-benzyl-S)-Y-L is the enzyme cleavable peptide and that γ-E-P-L-G is provided as SEQ ID NO 52. The use of this language is explained above and is considered to be correct.

Please call the undersigned attorney if further discussion on this aspect of the response is warranted.

Applicants gratefully acknowledge the comments that the proposed amendments to the claims filed August 15, 2003, had they been entered, would have overcome the rejections under 35 USC 112, second paragraph, and the prior art rejections set forth in the final Office action mailed May 8, 2003. These amendments and the argument presented therewith are included below with this response.

Rejections Under 35 U.S.C. § 112, second paragraph

Claim 4-9 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, in claim 4, the final R group is unclear because it contains bonds at both ends of the substituent. This is also found in Claims 5 and 30.

Applicants have amended each of these claims in order to overcome the 112, 2nd paragraph rejections. The final R group in Claims 4 and 5 has been removed and Claim 30 has been cancelled and replaced with new Claim 40 wherein this group has not been included. These amendments are considered to put these claims in condition for allowance.

Rejections Under 35 U.S.C. § 102(b), 102(e) and 35 U.S.C. § 103(a)

The examiner has noted that instant claims 1-32 and 35-39 are deemed not to be entitled under 35 U.S.C. § 119(e) to the benefit of the filing date of provisional application 60.189,387 because the provisional application, under 35 U.S.C. § 112, 1st paragraph, does not disclose, e.g., all of the E^{cp} groups recited in the instant claims. The examiner notes that Trouet et al., U.S. Patent No. 5,962, 216 is therefore available as prior art against the instant claims under 35 U.S.C. § 102(b).

Applicants respectfully disagree that the subject claims are not entitled to the benefit of the provisional filing date. However, in view of the following remarks, Trouet et al. is not considered to be relevant prior art against the instant claims.

Claims 1 and 2 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Trouet et al. The examiner notes that Trouet et al. teach the prodrug compound Gly-Leu-Gly-Leu-DNR. This compound, the examiner notes, corresponds to Applicants' claimed compound in which E^{cp} is Cap-Gly-Xp1-Xp2-Laa where Cap is R, which is hydrogen.

Applicants respectfully traverse this ground of rejection and present the following comments. Nowhere in the specification or claims is R defined as hydrogen. Cap is defined as an N-terminus group selected from R-, Xa4 and R-Xa4. However, in order to expedite the prosecution of the application, a proviso has been added eliminating hydrogen as a capping group. This amendment of claim 1 is considered to overcome this ground of rejection.

In view of the foregoing, withdrawal of this ground of rejection is respectfully requested.

Claims 35-39 are rejected under 35 U.S.C. § 103 (a) as being obvious over Trouet et al. The examiner notes that the application of Trouet et al. is the same as in the 102(b) rejection of Claims 1 and 2. The examiner notes that while Trouet et al. does not teach administering the prodrug compound in combination with a pharmaceutically acceptable carrier in order to treat breast cancer/carcinoma, that it would be obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the prodrug of Trouet et al. to treat breast cancer/carcinoma. The examiner points out that it is desirable to treat such a disease and since Trouet et al. teaches that daunorubicin is released from its prodrug form by enzymes present in breast cancer/carcinoma cells, it would be obvious to one of ordinary skill in the art to administer the prodrug of Trouet et al. in combination with a pharmaceutically acceptable carrier since it is routine to administer therapeutic agent sin combination with pharmaceutically acceptable carriers for ease of storage, transportation, measurement and administration.

Applicants respectfully traverse this ground of rejection and provide the following comments. In view of the comments in response to the 102 (b) rejection, Applicants submit that since the compounds claimed in Claims 1 and 2 are novel, their use as claimed in Claims 35-39 would not be obvious over Trouet et al. Applicants submit that this ground of rejection should also be withdrawn.

Claims 1-14 are rejected under 35 U.S.C. § 103 (a) as being obvious over Trouet et as applied against Claims 1 and 2 above and further in view of WO Patent Application 00/64486. The examiner notes that Trouet et al. generally teach a terminal group W, especially succinyl, linked through a peptide Z to a therapeutic agent M, especially doxorubicin. The peptide Z is cleaved by enzymes secreted by the target cells to permit entry of the therapeutic agents into the target cells. Trouet et al., it is clearly noted by the examiner, do not teach a peptide Z which is cleavable by a matrix metalloproteinase and which corresponds to Applicants' elected E^{cp} group. The '486 application teaches an amino acid sequence Pro-Leu-Gly-Leu-Trp-Ala which is cleaved by matrix metalloproteinases. The examiner notes that the amino acid sequence of the '486 application corresponds to Applicants elected E^{cp} group as defined in instant Claims 1, 4, 5 and 10. The examiner concludes that it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the prodrugs of Trouet et al. using the amino acid sequence taught by the '486 application because Trouet et al's prodrugs can be formed using any peptide which is cleaved by an enzyme, and because the WO applications' amino acid sequence is described as being cleavable by an enzyme which is associated with the tumor cells which are to be treated by Trouet et al.

Applicants respectfully traverse the rejection and present the following comments. The elected E^{cp} group is Cap-Paa-Xa2-Gly-Xp1-Xp2-Laa-. The amino acid sequence taught in the '486 application does not correspond to Applicants' elected E^{cp} group. As argued above, R is not equal to H and as such takes the amino acid sequence taught in the '486 application outside the elected species. Additionally, claim 1 has been amended to specifically exclude succinyl as a substituent for Cap. Thus, without this crucial link, there is no basis for combining the references in order to render obvious the instant claims.

Applicants submit that the instant claims are not obvious over Trouet et al. in view of the WO 0064486 application and request that this ground of rejection be withdrawn.

Claims 1-5 and 35-39 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Monsigny et al. (U.S. Patent No. 4,703,107). The '107 patent, the examiner notes, teaches anti-tumoral prodrugs PHA-Gly-Gly-L-Arg-L-Leu-Daunorubicin and PHA Gly-Gly L-Arg-L-Leu-Adriamycin. The drugs are liberated from the prodrugs by proteases excreted from the tumoral cells. It is also noted that the prodrugs can be combined with

pharmaceutically acceptable carriers. The examiner points out that the prodrugs correspond to Applicants' claimed compound in which E^{cp} is Cap-Xa2-Gly-Xp1-Laa or Cap-Gly-Xp1-Xp2-Laa, where Cap is R, which is polyhydroxyalkanoyl.

Applicants respectfully traverse the rejection and present the following comments. Claim 1 has been amended to specifically exclude polyhydroxyalkanoyl as a Cap substituent. Support for this amendment is found in paragraph 0444 of the published specification. Clearly without this crucial piece, the '107patent cannot anticipate the instant claims. Applicants submit that this ground of rejection should be withdrawn.

Claims 1-14 and 35-39 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Firestone et al. (U.S. 2002/0147138 A1). The examiner notes that Firestone et al. teach the enzyme activated anti-tumor and anti-metastatic prodrug N-Cbz-Gly-Phe-Ala-Leu-doxorubicin. The peptide portion is noted to be capable of being cleaved by collagenase (IV) or elastase. The prodrug, the examiner states, corresponds to Applicants' claimed compounds in which E^{cp} is Cap-Gly-Xp1-Xp2-Laa. The examiner goes on to note that in view of the similarity in structure between the peptide portion of the prodrug of Firestone et al. and Applicants' claimed E^{cp} group, the prodrug of Firestone is deemed inherently to be cleavable by the matrixins specified in these claims. The examiner concludes that sufficient evidence of similarity is deemed to be present to shift the burden to Applicants to provide evidence that the claimed compounds are unobviously different than that of Firestone et al.

Applicants respectfully traverse the application and present the following comments. The examiner notes that Firestone et al. teach a particular prodrug containing N-Cbz as the amino protecting group. Claim 1 has been amended to delete N-Cbz from the definition of "Cap". This amendment is considered to overcome the rejection over Firestone and Applicants submit that the rejection under 35 U.S.C. § 102 (e) over Firestone et al. should be withdrawn.

Applicants acknowledge the examiner's comments that Claims 15-29 would be allowable if rewritten to overcome the claim objections set forth in the action and to include all of the limitations of the base claim and any intervening claims.

The examiner has also noted that Claim 30 limited to the elected SEQ ID NO would be allowable if rewritten to overcome the rejections under 35 U.S.C. § 112, 2nd paragraph, and to include all of the limitations of the base claim and any intervening claims. Claims 31-32 are objected to a being dependent upon a rejected base claim but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. It is acknowledged that the prior art of record does not teach or suggest an E^{cp} group having the structure of the elected SEQ ID NO.

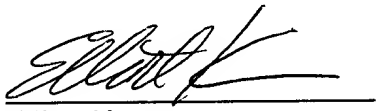
Claims 30-32 have been each cancelled and replaced with new claims 40-42 which are limited to the elected SEQ ID NO. These claims are considered to address the Examiner's comments and to put the application in condition for allowance.

In view of the foregoing, Applicants submit that the application, as amended, is in condition for allowance and courteously solicit a Notice of Allowance.

If any fee due is not accounted for herein, please charge such fee to Deposit Account No. 19-3880. If any extension of time is required and not petitioned for, such extension is hereby petitioned for, and it is requested that any fee due in connection therewith be charged to the aforementioned Deposit Account.

The foregoing amendment and response are believed to be fully responsive to the outstanding Office Action. If a direct personal communication would advance the prosecution of this application, please contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,



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Date: October 8, 2003

AMENDMENTS TO THE CLAIMS

Please amend claim 1 and add new claims 40-42 as follows:

Claim 1 (CURRENTLY AMENDED) A compound of Formula (I):

E^{cp}-A

(I)

or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide conjugated to A and selected from:

Cap- Paa -Xa2 -Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;

Cap- Xa2 - Sar - Xp1 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Sar - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is ~~an~~ natural amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, Cba, Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala, Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr, O-(C_1-C_4 alkyl)-Tyr, O-(phenyl(C_1-C_4 alkyl)-)-Tyr, (C_3-C_8 alkyl)-Gly, and aminoalkyl carboxylic acid;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is an amino capping group;

and

A is an antineoplastic agent;

with the following provisos:

a) Cap is not hydrogen;

b) Cap is not a polyhydroxyalkanoyl;

c) Cap is not a non-natural amino acid or succinyl;

d) Cap is not benzyloxycarbonyl (Cbz);

e) E^{cp} does not comprise a dipeptide linkage selected from -Tyr-Ser-; -Tyr-Thr-; -Phe-Ser-; -Gln-Ser-; -Gln-Thr-, and -Asn-Ser; and

f) E^{cp} is not -Gly-Gly-Arg-Leu- (SEQ ID NO: 4),

E^{cp} is not -Gly-Val-Phe-Arg- (SEQ ID NO: 5),

E^{cp} is not -Ala-Pro-Gly-Leu- (SEQ ID NO: 6),

E^{cp} is not 2-thienylalanine-Gly-Ala-Leu- ,

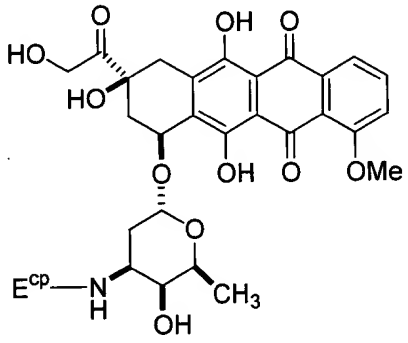
E^{cp} is not 2-naphthylalanine -Gly-Ala-Leu- , or

E^{cp} is not -Gly-Leu-Gly-Leu- (SEQ ID NO: 7).

Claim 2 (ORIGINAL) A compound of Claim 1 wherein A is doxorubicin, a doxorubicin derivative, or a doxorubicin analogue.

Claim 3 (ORIGINAL) A compound of Claim 2 wherein A is doxorubicin.

Claim 4 (CURRENTLY AMENDED) A compound of Claim 3 of Formula (Ia):



(Ia)

or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;

Cap- Xa2 - Sar - Xp1 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Sar - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, Cba, Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala, Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr, O-(C_1-C_4 alkyl)-Tyr, O-(phenyl(C_1-C_4 alkyl)-)-Tyr, (C_3-C_8 alkyl)-Gly, and aminoalkyl carboxylic acid;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)$-$(CH_2)_vC(=O)$-,

wherein v is 1, 2, 3, 4, 5, or 6;

H_3CO-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

HO_2CCH_2O-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

H_2N-$(CH_2CH_2O)_t$-$CH_2C(=O)$-, and

$H_3CC(=O)HN$-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

wherein t is 1, 2, 3, or 4;

R^1-$C(=O)$-;

R^1-$S(=O)_2$-;

R^1-$NHC(=O)$-;

R^{1a}-$CH_2C(=O)$-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4; and

2-carboxyphenyl-C(=O)-; ~~and~~

~~(O=)C-phenyl-C(=O)-~~;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or $-CO_2H$;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N-R^2$, $-SO_3H$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, $H_2N(C_2$-C_4 alkyl)-, acetyl(H)N(C_2-C_4 alkyl)-, or acetyl;

R^3 is -H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, phenyl, or benzyl;

R^4 is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N-R^2$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C_6-C_{10} carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

Claim 5 (CURRENTLY AMENDED) A compound of Claim 4 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;
Cap- Xa2 - Gly - Xp1 - Laa -;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;
Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;
Cap- Gly - Xp1 - Xp2 - Laa -;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -; and
Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;
Xa2 is an amino acid;
Xp1 is an amino acid wherein -Gly-Xp1- forms a bond cleavable by a matrixin;
Xp2 is an amino acid;
Xp3 is an amino acid;
Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, Cba, Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, Phe, Bip, Tyr, andO-benzyl-Tyr; and

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;
Xa4- is an amino acid;
R is selected from: $H_3CC(=O)$-;
$HOC(=O)$-$(CH_2)_vC(=O)$-,
wherein v is 1, 2, 3, or 4;
H_3CO-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,
HO_2CCH_2O-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,
H_2N-$(CH_2CH_2O)_t$-$CH_2C(=O)$-, and

$H_3CC(=O)HN$-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

wherein t is 1, 2, or 3;

R^1-$C(=O)$-;

R^1-$S(=O)_2$-;

R^1-$NHC(=O)$-;

R^{1a}-$CH_2C(=O)$-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4;

$HO_3SCH_2CH(NH_2)C(=O)$-; and

2-carboxyphenyl-$C(=O)$-; ~~and~~

~~(O=)C-phenyl-C(=O)-;~~

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or $-CO_2H$;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N$-R^2 , $-SO_3H$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, $H_2N(C_2\text{-}C_4$ alkyl)-, acetyl(H)N($C_2\text{-}C_4$ alkyl)-, or acetyl;

R^3 is -H, $C_1\text{-}C_4$ alkyl, $C_3\text{-}C_6$ cycloalkyl, phenyl, or benzyl;

R^4 is -OH, $C_1\text{-}C_3$ alkyl, $C_1\text{-}C_4$ alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N\text{-}R^2$;

$C_3\text{-}C_6$ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

$C_6\text{-}C_{10}$ carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

Claim 6 (ORIGINAL) The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

Claim 7 (ORIGINAL) The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

Claim 8 (ORIGINAL) The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin MMP-14.

Claim 9 (ORIGINAL) The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by MMP-2, MMP-9, and MMP-14.

Claim 10 (PREVIOUSLY AMENDED) A compound of Claim 5 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

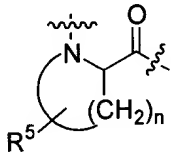
Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

wherein -Gly-Xp1- forms a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic of formula:  ; wherein R^5 is selected from H, halogen, C_1-C_6 alkyl, -OH, C_1-C_6 alkoxy, and benzyloxy; and n is 2, 3, 4, or 5;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp1 is an amino acid selected from Hof; Leu; Bip; Phe; nor-Leu; Tha; Phg; Val; Glu; Asn; Ser; Ala; homo-Tyr; Aze; 4-aza-Hof; O-(3-pyridyl)-Tyr; O-(4-pyridyl)-Tyr; O-benzyl-Tyr; O-benzyl-Thr; O-benzyl-Ser; O-methyl-Ser; O-allyl-Ser; 4-nitro-Hof; N-methyl-Leu; O-(4-pyridylmethyl)-Tyr; 4-hydroxy-phenyl-Gly; phenylpropyl-Gly; styryl-Ala , and 2Nal;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Xp3 is an amino acid selected from Tyr, Ala, Ser, Leu, Hof, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, and Val;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, Cba, Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, and Phe;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, Dmg, Ala, Arg, Asn, Asp, β-Asp, Aze, Cha, Cys, Dpa, Gln, Glu, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Sar, Ser, Thr, Trp, Tyr, and Val;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;
2-carboxycyclopentyl-C(=O)-;
carbobenzyloxy;
4-methoxy-benzenesulfonyl;
cyclopropylcarbonyl;
cyclobutylcarbonyl;
3-pyridinecarbonyl;
2-pyrazinecarbonyl;
tetrazoleacetyl;
pivaloyl;
methoxyacetyl;
hydroxyproline; and
4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Claim 11 (ORIGINAL) The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

Claim 12 (ORIGINAL) The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

Claim 13 (ORIGINAL) The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin MMP-14.

Claim 14 (ORIGINAL) The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by MMP-2 , MMP-9, and MMP-14.

Claim 15 (CURRENTLY AMENDED) A compound ~~of Claim 10~~ of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Leu - Laa -;
Cap- Paa - Xa2 - Gly - Hof - Laa -;
Cap- Xa2 - Gly - Leu - Laa -;

Cap- Xa2 - Gly - Hof - Laa -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Xa2 - Gly - Leu - Xp2 - Laa -;

Cap- Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Gly - Leu - Xp2 - Laa -; and

Cap- Gly - Hof - Xp2 - Laa -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Laa is an amino acid selected from Leu, Cha, Nle, and Hol;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Claim 16 (ORIGINAL) The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

Claim 17 (ORIGINAL) The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

Claim 18 (ORIGINAL) The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

Claim 19 (ORIGINAL) The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

Claim 20 (PREVIOUSLY AMENDED) A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Leu - Leu -;
Cap- Paa - Xa2 - Gly - Leu - Cha -;
Cap- Paa - Xa2 - Gly - Leu - Nle -;
Cap- Paa - Xa2 - Gly - Leu - Hol -;
Cap- Paa - Xa2 - Gly - Hof - Leu -;
Cap- Paa - Xa2 - Gly - Hof - Cha -;
Cap- Paa - Xa2 - Gly - Hof - Nle -;
Cap- Paa - Xa2 - Gly - Hof - Hol -;
Cap- Paa - Xa2 - Gly - Leu - Xp2 - Leu -;
Cap- Paa - Xa2 - Gly - Leu - Xp2 - Cha -;
Cap- Paa - Xa2 - Gly - Leu - Xp2 - Nle -;
Cap- Paa - Xa2 - Gly - Leu - Xp2 - Hol -;
Cap- Paa - Xa2 - Gly - Hof - Xp2 - Leu -;
Cap- Paa - Xa2 - Gly - Hof - Xp2 - Cha -;
Cap- Paa - Xa2 - Gly - Hof - Xp2 - Nle -; and
Cap- Paa - Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-; and

tetrazoleacetyl.

Claim 21 (ORIGINAL) The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

Claim 22 (ORIGINAL) The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

Claim 23 (ORIGINAL) The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

Claim 24 (ORIGINAL) The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

Claim 25 (PREVIOUSLY AMENDED) A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Xa2 - Gly - Leu - Leu -;
Cap- Xa2 - Gly - Leu - Cha -;
Cap- Xa2 - Gly - Leu - Nle -;
Cap- Xa2 - Gly - Leu - Hol -;
Cap- Xa2 - Gly - Hof - Leu -;
Cap- Xa2 - Gly - Hof - Cha -;
Cap- Xa2 - Gly - Hof - Nle -;
Cap- Xa2 - Gly - Hof - Hol -;
Cap- Xa2 - Gly - Leu - Xp2 - Leu -;
Cap- Xa2 - Gly - Leu - Xp2 - Cha -;
Cap- Xa2 - Gly - Leu - Xp2 - Nle -;
Cap- Xa2 - Gly - Leu - Xp2 - Hol -;
Cap- Xa2 - Gly - Hof - Xp2 - Leu -;
Cap- Xa2 - Gly - Hof - Xp2 - Cha -;
Cap- Xa2 - Gly - Hof - Xp2 - Nle -; and
Cap- Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn,

Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-; and

tetrazoleacetyl.

Claim 26 (ORIGINAL) The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

Claim 27 (ORIGINAL) The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

Claim 28 (ORIGINAL The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

Claim 29 (ORIGINAL) The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

Claims 30-34 (CANCELLED)

Claim 35 (ORIGINAL). A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

Claim 36 (PREVIOUSLY AMENDED). A method of treating a mammal afflicted with a cancer comprising administering to a mammal afflicted with a cancer a therapeutically effective amount of a compound of Claim 1.

Claim 37 (ORIGINAL). The method of Claim 36, wherein the cancer is a breast, ovarian, brain, stomach, lung, colon, prostate or liver cancer or wherein the cancer is a leukemia, lymphoma, carcinoma, sarcoma, or melanoma.

Claim 38. (ORIGINAL) A method of delivering a compound to the cells of a mammal afflicted with a cancer comprising contacting the cells of a mammal afflicted with a cancer with a compound of Claim 1, wherein the contacting is in the presence of a peptidase comprising a matrixin.

Claim 39 (ORIGINAL). The method of Claim 38, wherein the cancer is a breast, ovarian, brain, stomach, lung, colon, prostate or liver cancer or wherein the cancer is a leukemia, lymphoma, carcinoma, sarcoma, or melanoma.

Claim 40 (NEW) A compound of Claim 4 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;

(γ-E -P-L-G is provided as SEQ ID NO: 52)

R is selected from: $H_3CC(=O)$-;

$HOC(=O)$-$(CH_2)_vC(=O)$- ;

wherein v is 1, 2, 3, 4, 5, or 6;

H_3CO-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

HO_2CCH_2O-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

H_2N-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ; and

$H_3CC(=O)HN$-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

wherein t is 1, 2, 3, or 4;

R^1-$C(=O)$-;

R^1-$S(=O)_2$-;

R^1-$NHC(=O)$-;

R^{1a}-$CH_2C(=O)$-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4; and

2-carboxyphenyl-$C(=O)$-;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO_2H;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or -CO_2H;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO_2H; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, -CO_2H, -$N(CH_2CH_2)_2N$-R^2 , -SO_3H;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, $H_2N(C_2\text{-}C_4$ alkyl)-, acetyl(H)N(C_2-C_4 alkyl)-, or acetyl;

R^3 is -H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, phenyl, or benzyl;

R^4 is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N\text{-}R^2$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C_6-C_{10} carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

Claim 41 (NEW) A compound of Claim 40 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;

(γ-E -P-L-G is provided as SEQ ID NO: 52)

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Claim 42 (NEW) A compound of Claim 40 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;

(γ-E -P-L-G is provided as SEQ ID NO: 52)

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-; and

tetrazoleacetyl.